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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/621,684	07/17/2003	Scott A. Waldman	TJU-2858	1770

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EXAMINER	
PONNALURI, PADMASHRI	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 05/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/621,684	WALDMAN, SCOTT A.	
	Examiner	Art Unit	
	Padmashri Ponnaluri	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/20/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of Group I (new claims 23-44), and species election of peptide having amino acid sequence of SEQ ID NO: 2 as the ST receptor binding ligand, and 5-fluorouracil as the species of active agent, in the reply filed on 02/01/05 is acknowledged. Applicants response to the restriction requirement addresses that the instant claim composition includes both conjugated and unconjugated compositions. Applicant's response has been considered and the instant claim pharmaceutical compositions are considered to include both conjugated and unconjugated compositions. No restriction between the conjugated or unconjugated compositions has been made.

2. The amendment filed on 2/1/05 has been fully considered. Claims 1-22 have been canceled and new claims 23-44 have been added.

Priority

3. This application is a continuation of 09/263,477, which is a continuation of 08/583,447, which is a continuation-in-part of 08/141,892.

4. Claims 25, 32, and 43 recite SEQ ID NO: 55 and 56 as the ST receptor binding ligand peptides, which were not disclosed in the parent applications, 08/141,892, filed on 10/26/93. In a continuation-in-part application, only claims directed solely subject matter adequately disclosed under 35 USC 112, first paragraph in the parent application is entitled to the benefit of the filing date of the parent application. Thus, the instant claims 25, 32, 43, which recite sequences not disclosed in the parent applications are entitled only to the filing date of the continuation-in-part application. See MPEP 201.22.

Information Disclosure Statement

5. The references cited in the Information Disclosure Statement filed on 8/20/03 have been fully considered.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 23-25, 28-32, 35-37, 39, 41-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for ST receptor binding ligand with Sequence of SEQ ID NO" 2, 3 and 5-56, does not reasonably provide enablement for fragments and derivatives of such peptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant claims recite a pharmaceutical composition comprising: a ST receptor binding ligand and a radiostable active agent.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, unpredictability in the art, the amount of experimentation required, and the amount of direction or guidance presented.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation. Besides the peptides with amino acid sequence of SEQ ID Nose: 2, 3, 5-56, the specification fails to provide guidance

as to how to determine the peptides which are fragments and variants of the peptides. The specification defines that the polypeptide '*fragments*' as peptides, which has amino acid sequence identical to a portion of ST receptor binding ligand; and defines the polypeptide '*derivatives*' as a peptide, which has amino acid substantially identical to at least a portion of ST receptor binding ligand. The specification does not define the size of the 'polypeptide fragment' or how the 'polypeptide derivatives are derived. The specification discloses amino acid sequences SEQ ID NO: 2, 3, and 5, and fragments of SEQ ID NO: 2, SEQ ID NO: 3, and SEQ ID NO: 5. The specification does not disclose any other derivatives of ST receptor binding ligand. Despite knowledge in the art for producing polypeptide fragments and derivatives, the specification fails to provide guidance regarding what deletions from or alterations in the disclosed sequences result in polypeptide fragments and derivatives of SEQ ID NO: 2, 3 or 5.

Furthermore, while recombinant techniques are available, it is not routine in the art to screen large numbers of polypeptide fragments or variants where the expectation of retaining similar function (ST receptor binding property) is unpredictable based on the instant disclosure. Based on the specification disclosure predicting which amino acid fragments and derivatives would maintain function is well outside the realm of routine experimentation; thus a skilled artisan would require guidance, such as information regarding the size, and sequence of deletions and alterations which preserve the activity. Thus, it would require undue experimentation of one skilled in the art to practice the claimed invention. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, it would take undue trials and errors to practice the claimed invention.

8. Claims 23-25, 28-32, 35-37, 39, and 41-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is Written Description Rejection.

The instant claims recite a pharmaceutical composition comprising: a ST receptor binding ligand and a radiostable active agent.

The specification discloses St receptor binding ligand is a ST receptor binding peptide of sequence SEQ ID NO: 2, 3, and 5-56 and fragments and derivatives. The specification discloses ST receptor binding peptides with amino acid sequence of SEQ ID NO: 2, 3 and 5 and fragments and derivatives of the sequences of SEQ ID NO: 2, 3 and 5 (SEQ ID NO: 6-56). The specification has not disclosed fragments or derivatives of peptide sequences of SEQ ID NO: 6-56. The specification does not teach any other compounds as the ST receptor binding ligands. However, claims 23-25, 28-32, 35-37, 39, 41-43 directed to encompass fragments and derivatives to SEQ ID No: 6-56, and sequences from other species, mutated sequences, sequences that have a recited degree of identity (similarity, homology), and so forth. None of these sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry,

whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO: XXX, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmacentical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it

obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

Therefore, only SEQ ID NO: 2, 3, 5-56 but not the full breadth of the claim meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 23-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 23-44 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the carrier or diluent present in pharmaceutical compositions. In absence of the carrier that the instant pharmaceutical compositions would be same as a compositions. Applicants are requested to amend the claims to include the pharmaceutically acceptable carriers or diluents, or diluents.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for

patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 23-27 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent 4,490,080 (Duflot et al).

The instant claims recite a pharmaceutical composition comprising: a ST receptor binding ligand and a radiostable active agent.

Duflot et al disclose conjugates comprising ST receptor binding moiety (i.e., see claims 1-34) and a carrier agent (toxin) (i.e., see claims 21-34). The reference discloses ST receptor binding peptides comprising 18 amino acids of sequence Asn-Thr-Phe-Tyr-Cys-Cys-Glu-Leu-Cys-Cys-A-Pro-Ala-Cys-Ala-Gly-Cys-T, in which A and T each represent Tyr or Asn, and A and T are not the same (i.e., see Abstract or claim 1), which reads on the SEQ ID NO: 2, 3 of the instant claims. The reference claim 33 discloses the pharmaceutical compositions (inject able). The reference clearly anticipates the claimed invention.

12. Claims 23-24 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent 4,411,888 (Klipstein et al).

The instant claims recite a pharmaceutical composition comprising: a ST receptor binding ligand and a radiostable active agent.

Klipstein et al disclose conjugates and pharmaceuticals (i.e., see claims) comprising synthetic ST (refers to the ST receptor binding ligand of the instant claims) linked to cholera toxin. Thus, the reference clearly anticipates the claimed invention.

Double Patenting

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 23-44 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 of U.S. Patent No. 5,518,888. Although the conflicting claims are not identical, they are not patentably distinct from each other because the reference patent claim method discloses the use of pharmaceutical composition comprising a ST receptor binding moiety and an active moiety. And further the reference patent claims further recite that the ST receptor binding moiety is a peptide of SEQ ID NO: 2, 3, 5, 6 and SEQ ID NO: 54, which would read on the instant claim peptides. Further the reference modes of

administration of the pharmaceutical composition is within the scope of the presently claimed invention.

15. Claims 23-44 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-58 of U.S. Patent No. 5,879,656. Although the conflicting claims are not identical, they are not patentably distinct from each other because the reference patent claim method discloses the use of pharmaceutical composition comprising a ST receptor binding moiety and an active moiety. And further the reference patent claims further recite that the ST receptor binding moiety is a peptide of SEQ ID NO: 2, 3, and 5-56, and fragments and derivatives thereof, which would read on the instant claim peptides. Further the reference method claim modes of administration of the pharmaceutical composition is within the scope of the presently claimed invention.

16. Claims 23-28, 41-42 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 5,962,220. Although the conflicting claims are not identical, they are not patentably distinct from each other because the reference patent claim discloses pharmaceutical compositions comprising peptides as ST receptor binding moiety, and antisense molecule as active moiety, which would read on the therapeutic agent of the instant claims, and the modes of administration of the reference is within the scope of the presently claimed invention.

17. Claims 23-28 and 41-42 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,060,037. Although the conflicting claims are not identical, they are not patentably distinct from each other because the reference patent claim discloses pharmaceutical compositions comprising peptides as

ST receptor binding moiety, and the reference active moiety is a therapeutic agent, which would read on the therapeutic agent of the instant claims, and the modes of administration of the reference is within the scope of the presently claimed invention.

18. Claims 23-28 and 41-42 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 of U.S. Patent No. 6,087,109. Although the conflicting claims are not identical, they are not patentably distinct from each other because the reference patent claim discloses pharmaceutical compositions comprising peptides as ST receptor binding moiety, and antisense molecule as active moiety, which would read on the therapeutic agent of the instant claims, and the modes of administration of the reference is within the scope of the presently claimed invention.

19. Claims 23-25, 28-32, 35-36, 41-42 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 6, 8, 10, 32, 37, 9, 41-42, 54-55, 58, 63-64, 92, 96-97, 99, 102, 108, 109, 114, 116, 118-119, 125-153 of copending Application No. 08/468,449. Although the conflicting claims are not identical, they are not patentably distinct from each other because the reference pharmaceutical composition (i.e., claims 10, 32, 63) comprises a conjugated compound comprising an ST receptor binding moiety, and an active moiety, which read on the instant claim. The reference claim 32 does not specifiy that the ST receptor binding moiety is an antibody, thus it reads on the instant claim peptides as ST receptor binding moiety of the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner is on Increased Flex Schedule and can normally be reached on Monday through Friday between 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Padmashri Ponnaluri
Primary Examiner
Art Unit 1639

26 April 2005

PADMASHRI PONNALURI
PRIMARY EXAMINER